

Nucleic acids (NA) and nucleotides are basic components of every cell. Therefore, it is not surprising that the literature data show that most foods, both raw and highly processed, are a source of NA in the human diet. Nevertheless, in the field of food science, NA are perceived mainly in terms of their role as carriers of genetic information and their nutritional value is often ignored. This tendency is slowly changing, and in recent years, there has been a growing number of scientific reports suggesting the importance of nutritional role of NA. For example, NA and their components, due to their positive impact on the development of the immune system and the regeneration of the digestive tract, are recommended as supplements for infants and adults, and also for stock animals. The market of dietary supplements containing NA or nucleosides is developing very fast, despite the lack of structured knowledge about their nutritional role and the lack of nutritional recommendations regarding dietary NA.

Another insufficiently studied aspect of NA from a nutritional perspective is that they can undergo chemical modifications during food processing similarly as other nutrients such as lipids, proteins and saccharides. Due to redox-active chemical nature, NA and their components are susceptible to oxidation. Additionally, oxidation may be stimulated by higher temperature during thermal processing and the presence of other oxidized food ingredients. For example, red meat is subjected to high-temperature processing prior to its consumption and it has high content of heme iron, whose presence induces a number of oxidation reactions. In scientific literature, oxidized forms of lipids and proteins generated in the presence of heme iron have been linked to the carcinogenic properties of processed red meat. There are thus indications that oxidized dietary NA are potential source of toxicological risk, if the modified nucleotides derived from them are absorbed from the gastrointestinal tract and got incorporated into the consumer's DNA. So far, there are no published results of studies addressing this topic that would allow to verify such assumptions.

The aim of the proposed project is to investigate how heat treatment and heme iron content influence the formation of NA oxidation products in the selected meat samples and to investigate by means of biological tests whether exposure to modified NA and their components have a harmful effect on the cells of the gastrointestinal tract. The increased activity of the enzyme MTH1 triphosphatase in cells of gastrointestinal tract is an indirect indicator that modified nucleotides are a potential risk factor. This enzyme hydrolyses triphosphates linked to oxidized purine nucleotides found in the intracellular nucleotide pool. Triphosphatase MTH1 is believed to be a part of a system preventing the incorporation of oxidized nucleotides into the synthesized DNA. Oxidized nitrogenous bases in the DNA sequence can lead to mutations, and these are a recognized cause of cancer development. There is a risk that mentioned protective mechanisms may turn out to be insufficient upon a significantly increased exposure of gastrointestinal cells to oxidized NA.

The project initially aims at the qualitative and quantitative determination of NA oxidation products formed during heat treatment of meat. Meat samples that differ in the content of heme iron are selected for testing. Then, biological tests will be performed using cellular models of the human gastrointestinal tract which is in direct contact with the digested food components. The cytotoxicity and genotoxicity of the oxidized NA and their components will be investigated. The results of biological tests performed in cellular models with either normal or inhibited activity of MTH1 enzyme will be compared. The proposed research is expected to provide currently not available experimental data that could address the question whether oxidatively modified dietary NA should be considered as toxicological risk factor.